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Neointimal Hemorrhage After Drug-Eluting Stent Implantation

Possible Role for Development of Neoatherosclerosis

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A 57-year-old man died of sepsis, and an autopsy was performed. He had undergone percutaneous coronary intervention of the right coronary artery with paclitaxel-eluting stent implantation 43 months before death. Postmortem ex vivo intravascular ultrasound (IVUS) (Terumo Corp, Tokyo, Japan), optical coherence tomography (OCT) (St. Jude Medical, St. Paul, Minnesota), and pathological examination were carried out at the stented segment. IVUS and OCT images illustrated neointimal hyperplasia, leading to moderate luminal narrowing. IVUS clearly showed the hypoechoic mass within the neointima on the stent struts (Figure 1A, asterisks). OCT indicated neointimal hyperplasia with rapid attenuation of the signals (Figure 1B, asterisks). Both intravascular images suggested the presence of neoatherosclerosis after drug-eluting stent implantation (1).

Pathological evaluation demonstrated massive hemorrhage within the neointimal hyperplasia (Figure 2A). This striking feature could not be identified by intravascular imaging, such as IVUS and OCT. High-magnification view of neointima showed the foam cell infiltration with red blood cells (Figure 2B).

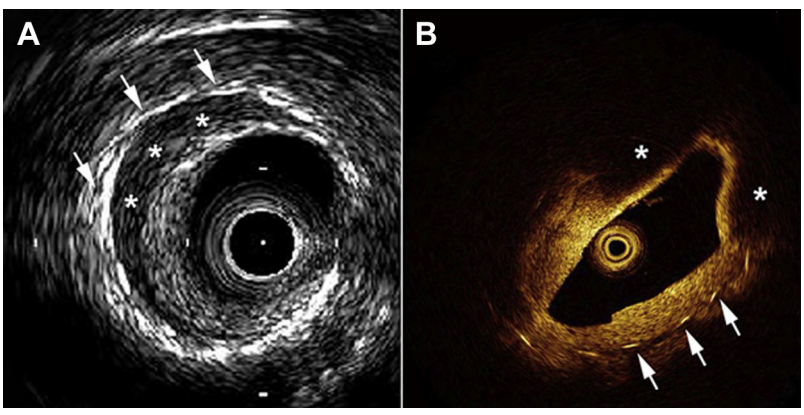

FIGURE 1 Postmortem Ex Vivo IVUS and OCT Images After Paclitaxel-Eluting Stent Implantation

(A) Intravascular ultrasound (IVUS) showed the hypoechoic mass **(asterisks)** within the neointima on the stent struts **(arrows)**. **(B)** Optical coherence tomography (OCT) demonstrated neointimal hyperplasia with rapid attenuation of the signals **(asterisks)**. **Arrows** indicate stent struts. These images suggested the presence of neoatherosclerosis after drug-eluting stent implantation.

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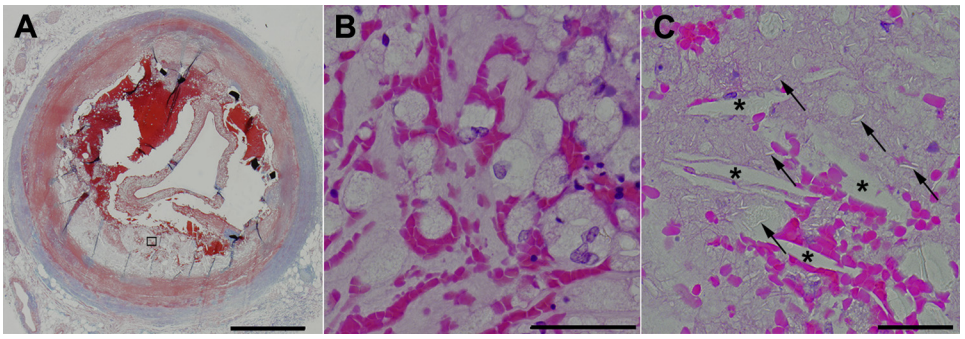

FIGURE 2 Histological Findings of Segment With Paclitaxel-Eluting Stent Implantation 43 Months Before Death

(A) Concentric neointimal hyperplasia with massive hemorrhage was apparent at the stented segment (Masson's trichrome stain, scale bar = 1μm). **(B)** High-magnification view of neointima directly under the lumen showed the foam cell infiltration with red blood cells (hematoxylin and eosin stain, scale bar = 50 μm). **(C)** High-magnification view of the **boxed area** in **panel A** demonstrated the presence of tiny cholesterol clefts **(arrows)** with large clefts **(asterisks)** within the neointima (hematoxylin and eosin stain, scale bar = 50 μm).

Although these foam cells existed directly under the vessel lumen, there was no histological evidence of plaque rupture and thrombus formation. Histological observation indicated the presence of tiny cholesterol clefts within the neointima (**Figure 2C**, arrows).

It is known that the plasma membrane of red blood cells is the important source of cholesterol esters in the vessel wall (2). In this case, massive hemorrhage within the neointima was observed, and red blood cells were adjacent to the tiny cholesterol clefts. Although large cholesterol clefts might penetrate from underlying plaque, the tiny cholesterol clefts, which are not commonly observed in the atherosclerosis of native coronary arteries, might be derived from the red blood cell membrane within the neointima.

These histological findings indicate the important role of hemorrhage for the lipid accumulation within the neointima. We might need to assume the distinct pathway for the development of neoatherosclerosis after drug-eluting stent implantation, which seems to progress more rapidly compared with that of atherosclerosis of native coronary arteries.

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